DEPARTMENT OF HEALTH & HUMAN SERVICES

M3091n

Food and Drug Administration
Denver District Office
Building 20 – Denver Federal Center
P.O. Box 25087
Denver, Colorado 80225-0087
TELEPHONE: 303-236-3000

October 15, 1999

**WARNING LETTER**

**CERTIFIED MAIL**
**RETURN RECEIPT REQUESTED**

Mr. Hansjoery J. Wyss
Chairman and CEO
1690 Russell Road
Paoli, PA 19301

PURGED

Ref # : DEN-00-01

Dear Dr. Wyss:

During an inspection of your firm located at 1051 Synthes Avenue, Monument, Colorado on July 12 - 23, 1999 and August 2 - 6, 1999, 1999, Consumer Safety Officer Thai Duong determined your firm manufactures Class II implantable screws, nails, plates, and various Class I instruments. These products are devices within the meaning of Section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

The above-stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for the manufacturing, packing, storage, or installation are not in conformance with the Quality System Regulation (QSR), as specified in Title 21, Code of Federal Regulations, Part 820 (21 CFR 820) as follows:

1. Production processes were not always controlled or monitored to ensure that devices conformed to their specifications [21 CFR 820.70] and in-process/final acceptance activities were not always controlled to ensure specified requirements were met [21 CFR 820.80]. Devices, including implantable screws, nails and plates and various instruments, failed to meet specifications prior to release for distribution. Customer complaints listed in the examples below were received and verified. (repeat violation)

Dimensional:
Complaint [redacted] dated 2/25/99, 456.90 TI Spiral Blade 90mm – "...package is labeled #456.90 – 90mm length. Blade is etched with #456.90 – 90mm length. However, blade measures 95mm in length."

Complaint [illegible] dated 2/11/99, 313.833 1.5mm Screwdriver Blade/slf-rtg/Stardrive/Long – "Product is labeled 313.833 (1.5mm/Long) and color-coded red but the actual product contained in the package was 313.843 (2.0mm/Long)."

Complaint [illegible] dated 11/17/98, 209.070 7.0mm Cann Screw 32mm Thread x 70mm – "...32mm Thread, but inside the package was a 7.0 Cannulated Screw with 16mm threads." Complaint resulted in a Class III recall.

Mislabeled:
Complaint [illegible] dated 12/7/98, 209.695 7.3mm Cannulated Screw – "One of the screws is 65mm, but labeled 95mm in length." "...product was in fact labeled incorrectly."

Complaint [illegible] dated 8/10/98, 421.096 Box Plate – "...the product contained in the package does not match ..." Product was mislabeled with other product's label. Complaint resulted in a Class III recall.

Complain[illegible] dated 3/11/98, 400.812.96 1.5mm Ti Self-Tapping Screw 12mm – "Received screws with the label as blue." Blue labels were for 2.0mm screws. This complaint resulted in a Class III recall.

Misanodized:
Complaint [illegible] dated 7/13/98, 447.515 2.0mm Ti L-Plate Malleable, Right – "The part should be anodized gray/green, but the anodize color is gold." Complaint resulted in a Class III recall.

Complaint [illegible] dated 7/13/98, 446.516 2.0mm Ti L-Plate Malleable, Left – "The parts should be anodized gray/green, but the anodize color is gold." Complaint resulted in a Class III recall.

Product Investigation Form with Product Action Number (PAN) 99020401, 1.5mm Ti Y-Plate – "Parts are anodized gold, the part should be anodized green/gray." This resulted in a Class III recall.

Misetched:
Complain[illegible] dated 4/19/99, 309.039 Extraction Bolt f/3.5mm & 4.0mm Screws – "... Extraction Bolts are miseched." This resulted in a Class II recall.

Complaint [illegible] dated 8/21/98, 456.011 110 Deg Specialty Locking Sleeve F/Ti Femoral Nail – "...456.012 was etched as a 456.011."

Complaint [illegible] dated 3/20/98, 280.325 DHS/DCS One-Step Lag Screw 125mm – "Part was etched with wrong length."

Wrong/missing insert:
Product Investigation Form with Product Action Number (PAN) 98072001, 475.935S 3.5mm Sterile Ti Elastic Nail 440mm – "Product contains the wrong insert (GP0735)." This resulted in a Class II recall.

PURGED

DHRs with Lot A6G7403 and A6G6911 with completed date 2/9/98 for part 356.982 4.0mm Three-Fluted Calibrated Drill Bit – show products were repacked and relabeled with inserts. The discrepancy was found in-house that the product did not contain the required insert. This resulted in a Class II recall.

Packaging:
Complaint [redacted] dated 5/6/99, 214.836 4.5mm Self-Tap Cortex Screw 36mm – "...received an empty package."

Complaint [redacted] dated 8/19/98, 351.76S 3.0mm Reaming Rod W/ Straight Ball Tip Sterile – "The reaming rod received bent." "... instructed not to use unapproved alternate packaging."

Complaint [redacted] dated 2/1/99, 241.36 One Third Tubular Plate W/Collar-6 Holes/73mm – "...package was received empty."

2. Documented evidence was not always found that corrective and preventive actions were statistically detected, were identified, were verified/validated, changes were implemented/recorded in procedures, and information was disseminated [21 CFR 820.100(a)(1), (3)-(7)]. Review of corrective and preventive actions revealed the following:

   a) "Broke" was identified as one of most prominent problems in the complaint trending reports (4th quarter of 1998 and 1st quarter of 1999). No corrective and preventive action was taken.

   b) The action for the 4th quarter of 1998 complaint trending report was to establish goals for complaint action levels. Action levels were not established for the trending of product complaints by problem type.

   c) [redacted] was de-certified in 1/98, the issues and the corrective and preventive actions regarding the issues were not documented. There was no documented evidence to show that the issues were addressed.

   d) Complaint [redacted] dated 11/20/98, regarding bent drill bits received in its package, concludes that the "Product is so small and fragile that existing plastic bag is insufficient to protect product while stored and shipping." The action needed to correct and prevent recurrence of nonconforming product was not identified.

   e) Complaint [redacted] dated 11/5/98, regarding bent guide rod wire received in its package, states that a new triangular heavy pound test shipping carton to prevent transit damage was implemented in 1/99. There was no documented evidence to show the preventive action was implemented.

   f) The action for the 1st quarter of 1999 complaint trending report was to investigate causes and potential action to eliminate 2 screws in a bag. Pick/pack personnel to check bags for 2 per bag or empty bag was the proposed corrective action. The training of the personnel was not documented.

PURGED

3. Procedures for acceptance of incoming product were not always maintained and incoming product that did not meet specified requirements was not always accepted with appropriate documentation; or rejected [21 CFR 820(b)]. Review of incoming inspection revealed (repeat violation):

   a) Raw material, [illegible] lot 10659, was accepted although the material failed to conform to specifications stated in the DMR.

   b) Raw material, [illegible], lot 10223 was accepted although the material failed the first test, but passed the second test. There was no documentation to show that a second test was allowed.

4. The Device Master Records did not always include appropriate drawings with device specifications or production procedures [21 CFR 820.181(a)-(b)]. Review of Device Master Records (DMRs) revealed the following:

   a) The DMRs for Part #s 401.026 – 401.038, 2.0mm Cortex Screws with various lengths, did not contain or refer to the master drawing for these devices from 6/93 to 6/99. During this time period, the parts listed above were manufactured without a master drawing.

   b) Form F-M096 Rev. D was being used as the Device History Record for the products received from [illegible] The Device Master Record did not contain or refer to this form. For example: part # 310.25 and # 317.835.

5. Incoming product was not always inspected or tested as conforming to specified requirements [21 CFR 820.80(b)]. Certified Suppliers Work Instruction, dated 12/2/98, requires that once the supplier was de-certified, all future lots received would be sent to inspection. [illegible] was de-certified in 1/98, however, products received continued to be shipped directly from supplier to inventory with visual verifications.

6.A. Device History Records (DHRs) were not always maintained to assure the device was manufactured in accordance with the Device Master Record [21 CFR 820.184]. Review of DHRs for the drill bits received from [illegible] revealed the following:

   a) There was no documented evidence to show that the certificate of compliance was being reviewed for each lot. Example: Complaint [illegible], dated 4/27/98, 310.25 Drill Bit 2.5mm QC Brown, lot A6H0401 – '[illegible] reports drill bit broke while drilling." A review of the DHR noted heat treat for this lot was well within normal limits at [illegible]. The [illegible] with release date of 2/25/97 for this part, shows the hardness requirement of [illegible]. The heat treat for this lot did not meet specification and the lot was not rejected.

   b) Certificate of compliance received on a routine basis did not contain the required acceptance criterion (hardness). For example: part # 510.25, lot A6I2142, dated 7/7/99; part # 317.835, lot A6I0530, dated 6/26/99.

PURGED

c) The DHRs did not contain or refer to the label and the labeling used for the released lots. For example: part # 510.25, lot A6I0500, release date of 6/17/99; part # 317.835, lot A6I8112, release date of 7/12/99.

d) The results of acceptance or rejection of the hand written acceptance criteria were not documented. For example: Part # 317.835, lot A6H7238, release date of 4/7/99; part # 316.18, lot A6I8104, release date of 3/9/99.

6.B. Documents were not always approved and distributed by a designated individual [21 CFR 820.40(a)]. Review of Device History Records (DHRs) for the drill bits received from [illegible] revealed the following:

a) No predetermined acceptance criteria were specified on the form (F-M096 Rev. D), instead a hand written and unapproved acceptance criteria were used. For example: part #316.18, lot A6I8104, release date of 2/5/99; part #310.19, lot A6I0308, release date of 4/20/99.

b) A hand written acceptance criterion states 1.0 AQL Inspection on the DHR. It was unclear what was inspected. For example: part # 510.25, lot A6I1582, release date of 6/16/99; part #317.835, lot A6I8112, release date of 4/5/99.

7.A. Device History Records (DHRs) were not always maintained to assure the device was manufactured in accordance with the Device Master Record [21 CFR 820.184]. A review of [illegible] lots of the quarterly audits of Unique Instruments revealed:

a) Opened packages were repackaged or resealed without approval for release to finished goods. [illegible] of the [illegible] lots lacked approval for release.

b) [illegible] of the [illegible] lots were found that the entire lot needed to be repackaged and the reason to repackage the entire lot was not documented.

c) The DHR for Part # 310.48, lot A6H0148, lacked the required certificate of conformance for hardness and certificate of conformance of the raw material.

7.B. Documents were not always approved and distributed by a designated individual [21 CFR 820.40(a)]. For example, a review of [illegible] lots of the quarterly audits [illegible] revealed that opened packages used during incoming inspection were resealed in its own original packages. [illegible] of the [illegible] lots were resealed in its own packages and there was no approval for such process.

7.C. Changes to documents were not always reviewed and approved by a designated individual and change records did not always include a description of the change, identify the affected documents, include the signature of the approving individual, include the approval date, and include the effective date of the change [21 CFR 820.40(b)]. For example, a review of [illegible] lots of the quarterly audits of [illegible] revealed that [illegible] of the [illegible] lots were found with incoming inspection sheets modified. The inspection step was removed and an instrument was replaced for part # 317.861S, lot A6G9751.

PURGED

8. Review of the [illegible] which consisted of the software and hardware components necessary to [illegible] DHRs and maintain them as electronic records, revealed the following:

a) Changes to processes were not always reviewed and evaluated or revalidated, where appropriate, and documented [21 CFR 820.75(c)], in that the software validation dated [illegible] was completed for software [illegible] The current software [illegible] in use was [illegible]

b) There was no assurance that records could be retained for a period of time equivalent to the design and expected life of the device [21 CFR 820.180(b)], in that, it was not demonstrated that electronic copies of DHRs could be stored and retrieved for the duration of the record retention period.

c) Documents were not always approved and distributed by a designated individual [21 CFR 820.40(a)], in that, [illegible] of DHRs began in [illegible], and there was no documented approval that allowed the DHRs to be [illegible] In addition, the software validation was not completed until [illegible]

d) Documents were not always approved and distributed by a designated individual [21 CFR 820.40(a)], in that the policies and procedures, "[illegible]" and "[illegible]" dated 4/28/98, were the documents in use and they were not reviewed and approved.

9. Review of the firm's failure investigation of complaints revealed:

a) Non-conforming product was not always disposed or documentation justifying its use was not found [21 CFR 820.90(b)]. For example, complaint [illegible], dated 4/27/98, 310.25 Drill Bit 2.5mm QC Brown, lot A6H0401 – "[illegible] reports drill bit broke while drilling." A review of the DHR noted heat treat for this lot was well within normal limits at [illegible] The complaint was indeterminate. The [illegible] with release date of 2/25/97, for this part shows the hardness requirement of [illegible] The heat treat for this lot did not meet specification and the lot was not rejected.

b) Complaints involving the possible failure of a device were not always adequately investigated [21 CFR 820.198(c)]. For example, complaints [illegible] dated 2/6/98 and [illegible] dated 1/30/98 lacked hardness tests for the returned products. In addition, there was no justification for not performing the test.

c) Investigations of complaints involving the possible failure of a device were not always adequately documented [21 CFR 820.198(c)]. Complaints [illegible] and [illegible] dated 11/29/98 lacked results from the hardness tests performed.

PURGED

10. Packaging and shipping containers did not always ensure that damage to product did not occur during handling [21 CFR 820.130]. For example, there was no documentation to show that the plastic bag used to package the drill bit and its shipping container was designed to protect the device from alteration or damage during distribution.

11. Production processes were not always controlled or monitored to ensure that devices conformed to their specifications [21 CFR 820.70]. For example, a review of the gamma sterilization 4th quarter of 1998 and 1st quarter of 1999 quarterly audits revealed the minimum and maximum specified doses (illegible and illegible respectively) had a larger range than the established doses (illegible and illegible) in the original validation. The 1st quarter audit had an actual maximum dose received of (illegible)

12. Relevant information identifying quality problems, as well as corrective and preventive actions, were not always submitted for management review [21 CFR 820.100(a)(7)], in that corrective and preventive actions generated from the internal quality system audit were not submitted for management review.

13. Required activities in audit procedures were not always documented [21 CFR 820.22], in that the (illegible) procedure, (illegible) stated that an independent auditor prepare for the audit. There was no documented evidence to show the activity was performed.

For your information, during the inspection our Investigator also noted there is no assurance that the (illegible) could create an audit trail that was computer generated and time stamped to independently record the date and time of operator entries and action as required by 21 CFR 11.10(e).

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA-483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems you must promptly initiate permanent corrective actions.

You should take prompt action to correct these and any other manufacturing or quality systems deviations identified by your internal audits. Failure to promptly correct these deviations may be identified in a follow-up inspection, and may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

We have thoroughly reviewed your written responses dated August 20, September 21 and October 4, 1999, and considered your verbal responses provided during a September 30, 1999 meeting. Your responses do not adequately address the deficiencies observed during the inspection in that they do not ensure system-wide compliance with the QSR.

PURGED

Please notify this office in writing, within 15 days of receipt of this letter, of any additional steps you will be taking to achieve compliance, which have not been previously reported to us. Any response should address system-wide corrective actions, including time frames for completion.

Your reply should be sent to the Food and Drug Administration, Denver District Office, Attention: H. Tom Warwick, Compliance Officer, at the above address.

Sincerely,

Gary C. Dean
District Director

cc: Mr. James K. McCracken
Director of Compliance, Clinical & Regulatory Affairs
Synthes (USA) LTD.
1051 Synthes Ave.
Monument, CO 80132

PURGED

Mr. Thomas A. Freestone
Plant Manager
Synthes (USA) LTD.
1051 Synthes Avenue
Monument, CO 80132